REMARKS

Claimed Subject Matter

No amendments are presented in this response. Claims 12-14, 16-20, 22, 24-25, 27-28 and 30-35 remain pending in the application.

Rejection Under 35 U.S.C. § 112, First Paragraph

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. § 103

Claims 12-14, 16-20, 22-25, and 27-28 stand rejected under 35 U.S.C. §103(a) as being obvious over Breivik et al. (U.S. Pat. No. 5,502,077) in view of Garrison et al. (The Nutrition Desk Reference). The rejection is traversed for the reasons set forth below.

1. The Examiner has failed to establish a *prima facie* case of obviousness

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings of prior art references; and the references, when combined, must teach all of the claim limitations. See MPEP 2143. As defined in independent claims 12, 18, 24 and 27, the present invention is directed to the use of essential fatty acids with a high content in EPA-ethyl ester, DHA-ethyl ester or a high concentration mixture of EPA-ethyl ester and DHA-ethyl ester for the prevention of mortality or sudden death due to the reoccurrence of cardiovascular events in patients who have suffered from a myocardial infarction. As further described below, neither of the cited references remotely teaches or suggests the prevention of mortality or sudden death in a patient due to the reoccurrence of cardiovascular events. Thus, Applicants submit that the cited references do not provide the necessary motivation or suggestion to combine the reference teachings; and, even if combined, the references do not teach all of the claim limitations of the present invention.

As acknowledged by the Examiner, the principal reference, Breivik et al., differs from the present invention in that "Breivik et al. does not highlight the prevention of mortality caused by reoccurrence of cardiovascular events in a patient who has survived a myocardial infarction." However, the Examiner contends that the present invention is nonetheless obvious because Breivik et al. teach the prevention of risk factors which may lead to a cardiovascular disease which may then further lead to premature mortality. The Examiner further concludes that the selection of a specific patient population in whom to practice the prevention of cardiovascular risk factors is simply a matter within the purview of the skilled artisan because Garrison et al. list myocardial infarction as a "cardiovascular disease."

Applicants disagree with the Examiner's reasoning. The disclosure of Breivik et al. is limited to the study of hypertension, hypertriglyceridemia and high coagulation factor VII phospholipids complex activity in otherwise healthy patients having undetected moderate hypertension without previous cardiac illness or cardiac drug use. See Col. 6, lines 20-37 of the reference. Contrary to the Examiner's conclusion, patients without a history of cardiac illness as studied by Breivik et al. are entirely distinguishable from patients who have suffered a myocardial infarction as defined in the present invention. For example, it has been shown that 80% of patients who have survived a myocardial infarction exhibit low ventricular ejection fractions and are at high risk of sudden death from the reoccurrence of cardiovascular events. See page 4, lines 19-21 of the specification. Further, as described in Pfeffer, "Left Ventricular Remodeling in Acute Myocardial Infarction," Annu. Rev. Med. 46:455-66 (1995) (attached hereto as Appendix A), myocardial infarction "results in a prompt reduction in regional wall motion and often leads to more protracted and progressive changes in ventricular architecture." See abstract at 455. In particular, "patients who suffer an acute myocardial infarction are at greater risk of cardiac complications, including acute myocardial rupture. More commonly however, the clinical complications of infarct expansion are manifest in the long term by congestive heart failure, aneurysm formation, additional myocardial ischemic events, and premature cardiovascular mortality." Id. at 458. Accordingly, one skilled in the art would understand that patients having demonstrated and elevated risks for the reoccurrence of cardiovascular events after suffering a myocardial infarction would have significantly different

"cardiovascular risk factors" than a patient having undetected moderate hypertension without previous cardiac illness. Therefore, the teaching of Breivik et al. related to the prevention of hypertension, hypertriglyceridemia and high coagulation factor VII phospholipids complex activity in patients having undetected moderate hypertension without previous cardiac illness cannot be said to remotely teach or suggest the prevention of mortality or sudden death from the reoccurrence of cardiovascular events in patients who have suffered a myocardial infarction.

Further evidence that the class of patients having suffered from a myocardial infarction is distinguishable from otherwise healthy patients without previous cardiac illness is the fact that the American College of Cardiology and the American Heart Association have developed practice guidelines for the treatment of myocardial infarction. See, for example, Ryan et al., "ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction)," J Am Coll Cardiol 28:1328-1428 (1996); Ryan et al., "1999 Update: ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction," J Am Coll Cardiol 34:890-911 (1999); and Antman et al., "ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction: Executive Summary: A Report of the ACC/AHA Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines on the Management of Patients with Acute Myocardial Infarction)," Circulation 110:1-49 (2004). A copy of the 1996 Practice Guidelines is attached to this response as Appendix B; a copy of the 1999 Practice Guidelines is attached to this response as Appendix C and a copy of the 2004 Practice Guidelines is attached to this response as Appendix D. Because the ACC/AHA Practice Guidelines are designed particularly for the management of patients who have suffered a myocardial infarction, Applicants submit that one skilled in the art treating a patient who has suffered a myocardial infarction would refer to the Practice Guidelines rather than general references such as Breivik et al.

Further, it is important to note that the ACC/AHA Practice Guidelines in place at the time of the invention do not provide any discussion of the administration of omega-3 fatty acids to patients who have suffered a myocardial infarction. In particular, the 1996 and 1999 Guidelines outline a "rationale and approach to pharmacotherapy" and steps for "secondary prevention" in the management of patients who have suffered a myocardial infarction without any mention of the administration of n-3 fatty acids. See, for example, pages 1358-1400 of the 1996 Guidelines. It is not until the 2004 Practice Guidelines that omega-3 fatty acids are described as being of benefit for patients exhibiting a triglyceride level greater than 200 mg/dL. See, for example, pages 38-43 of the 2004 Guidelines. Thus, it is submitted that one skilled in the art at the time of the invention would not be motivated to administer fatty acids to patients who have suffered a myocardial infarction for the prevention of mortality or sudden death from the reoccurrence of cardiovascular events.

Because the teaching of the references is limited to the prevention of hypertension, hypertriglyceridemia and high coagulation factor VII phospholipids complex activity in otherwise healthy patients having undetected moderate hypertension without previous cardiac illness, and patients who have suffered a myocardial infarction are known to have increased risk of mortality or sudden death from the reoccurrence of cardiovascular events, Applicants submit that the cited references fail to provide any teaching or suggestion regarding the prevention of mortality or sudden death from the reoccurrence of cardiovascular events in patients who have suffered a myocardial infarction as required by the instant claims. Accordingly, the references lack the required motivation or suggestion for one skilled in the art to practice the present invention. Thus, Applicants submit that the Examiner has failed to establish a *prima facie* case of obvious such that claims 12-14, 16-20, 22-25, and 27-28 are patentable over Breivik et al. (U.S. Pat. No. 5,502,077) in view of Garrison et al. (The Nutrition Desk Reference). Reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is requested.

2. The Examiner is applying an improper "obvious to try" rationale

Applicants further submit that the Examiner is applying an improper "obvious to try" rationale for combining the references in support of the obviousness rejection. "An 'obvious to

try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. In re Eli Lilly & Co., 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). As described above, Breivik et al. teach the prevention of general cardiovascular risk factors including hypertension, hypertriglyceridemia and high coagulation factor VII phospholipids complex activity in otherwise healthy patients having undetected moderate hypertension without previous cardiac illness or cardiac drug use. Likewise, Garrison et al. generally described myocardial infarction as a "cardiovascular disease." Nothing in the cited references describes the prevention of mortality or sudden death from the reoccurrence of cardiovascular events in a patient who has suffered a myocardial infarction. Further, nothing in the reference provides any teaching with respect to the treatment of any patient having suffered a myocardial infarction or whether the administration of any of the compounds of the reference to such a patient would have any effect. Accordingly, Applicants submit that the cited references do not contain a sufficient teaching of how to prevent mortality or sudden death by the reoccurrence of cardiovascular events in a patient who has suffered a myocardial infarction such that the Examiner is applying an improper "obvious to try" rationale for combining the references to support an obviousness rejection. Reconsideration and withdrawal of the rejection is requested.

Conclusion

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot by this amendment. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 446-7683.

Applicants do not believe that any fee is required by the timely submission of this response. However, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 08-0750. Further, if there is any other fee deficiency or overpayment of

any fees in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or credit such overpayment to Deposit Account No. 08-0750.

Respectfully submitted,

James E. Davis, Reg. No. 47,516
Harness, Dickey & Pierce, P.L.C.
7700 Bonhomme, Suite 400
St. Louis, Missouri 63105
(314) 726-7500

JED/pml
Enclosures: Appendices A-D

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8

I certify that this correspondence is being deposited with the U.S. Postal Service on **August 20, 2004** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450**.

Peggy Marie Leslie